

1 CROSS-REFERENCE

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3 This application is a Continuation-In-Part of U.S. Patent Application Serial No.
4 09/855,468 filed May 15, 2001, ^{now abandoned} ~~now pending~~, and of International Patent Application No.
5 PCT/US00/18777 having an international filing date of 10 July, 2000, now pending.
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7 RESEARCH SUPPORT

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9 The research for the present invention was supported in part by grants from the
10 Multiple Sclerosis Society of Canada and the Canadian Myelin Research Initiative.
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12 FIELD OF THE INVENTION

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14 The present invention is concerned generally with glial cell components of the central
15 nervous system; and is particularly directed to in-vitro isolation of embryonic human
16 microglia ("HM") cells and establishment of immortalized human microglia ("HMO6") cells
17 and cell lines which are identifiable, stable, functionally active, and in continuous
18 proliferation in-vitro.
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20 BACKGROUND OF THE INVENTION

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22 Microglia are a major glial component of the central nervous system (CNS); play a
23 critical role as resident immunocompetent cells and phagocytic cells in the CNS [van Furth,

1 For these reasons, a variety of in-vitro assays and in-vivo therapeutic uses are
2 envisioned and intended for the present invention. These include the following:

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4 1. The immortalized human microglia cells can be used in-vitro to isolate neurotoxic or
5 neurotrophic molecules naturally produced by human microglia or produced in response to
6 inflammatory factors or neuroactive molecules such as β -~~amyloid~~ amyloid

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8 2. Because microglia have been implicated in neurological disorders, such as Alzheimer
9 disease, Parkinson disease, AIDS-dementia, ALS and MS, the immortalized human microglia
10 can be used for discovery (screening) of new drugs to treat the aforementioned conditions
11 and inflammation. Prospective drug candidates are those that can counter or reduce
12 production of proinflammatory cytokines, oxygen radicals, proteases such as caspase-3 and -
13 8, and neurotoxic agents such as β -amyloid.

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15 3. Human immortalized microglial cells can be further genetically manipulated to
16 express and produce additional proteins, peptides, or prodrugs. Such substances would
17 include a diverse range of chemokines, cytokines, and various marker proteins (e.g., LacZ
18 and GFP), growth factors, neurotrophic molecules, anti-apoptotic molecules (e.g., Bcl-2), and
19 enzyme inhibitors (e.g., caspase inhibitor). Microglia cells can be additionally genetically
20 modified to block the production of proteins that typically become overproduced by nervous
21 system pathologies. For example, upstream from the v-myc gene, there can be inserted an
22 activatable suppressor gene. Alternately, for human treatment, there can be inserted a suicide
23 gene.